REMARKS

Support for the above new claims is provided in the specification at least on page 7, lines 30-33. No new matter has been introduced and entry of the new claims is respectfully requested.

As an initial matter, Applicants believe that it would be helpful to briefly summarize the invention to which the claims are directed. The methods of the claimed invention essentially involve the acts of

> displaying peptide(s), that are capable of binding a proteinaceous target (claim 1) or antigen (claim 3) on the surface of replicable display package(s);
>
> synthesizing, on a solid phase, oligopeptides derived from a proteinaceous target; and
>
> contacting the display package(s) with the oligopeptides on the solid phase.

Claim 1 is directed to the use of these acts to identify displayed peptide(s) that bind to the oligopeptides while claim 3 is directed to the use of these acts to distinguish between displayed peptides that bind from those that do not bind (and would thus be "washed away" as recited in the claim).

The invention is thus generally applicable for practice in a variety of contexts by selecting the proteinaceous target(s) to be used followed by the synthesis of oligopeptides derived from the target(s) on a solid phase. This solid phase is then contacted with replicable display package(s) that display peptide(s) on their surface. There is no need to limit the invention to the particular structure or sequence of a proteinaceous target or particular displayed peptides because the invention is generally applicable to a variety of targets and a variety of displayed peptides to identify or distinguish peptides that bind and don't bind to a target (by virtue of binding or not binding to oligopeptides derived from the target).

Withdrawal of claims from consideration

The Office Action mailed May 20, 2002 withdrew claims 13-18 (submitted with the response filed March 1, 2002) from consideration "as being directed to a nonelected invention".

Applicants respectfully traverse because claims 13-18 are dependent from elected claim 3 **and** the Examiner has provided no basis for why they would be part of any non-elected group. The claims are directed to further exemplifications of the methods of elected claim 3 and would not require any serious burden of search for their consideration.

Applicants therefore respectfully request that claims 13-18 be considered on their merits.

Rejection under 35 U.S.C. § 112, first and second paragraphs

Claim 1 is rejected under 35 U.S.C. § 112, first and second paragraphs, as allegedly failing to provide sufficient "metes and bounds". Applicants have carefully reviewed the statement of this rejection and are confused as to whether this rejection is based on claim scope and enablement (35 U.S.C. § 112, first paragraph) or indefiniteness (35 U.S.C. § 112, second paragraph).

Applicants traverse, however, because a rejection based on either of those grounds would not be appropriate in the instant case. Claim 1 is directed to the identification of displayed peptides that bind a proteinaceous target by contacting the peptides with oligopeptides derived from the target and identifying whether the displayed peptides bind to the oligopeptides. If the displayed peptides bind the oligopeptides, they would be recognized as binding the target. There is simply no requirement that the actual structure or sequence of the proteinaceous target, of the oligopeptides derived therefrom, or the displayed peptides contacted therewith, be specified for the claim to be clear and enabled.

The claim is directed to encompassing the practice of the method regardless of what proteinaceous target is selected for derivation (and synthesis of oligopeptides) followed by contact with displayed peptides that may or may not bind the target. The rejection has provided no reasons why this is insufficiently enabled by the application as filed in light of skill in the art (to support a rejection under 35 U.S.C. § 112, first paragraph) or why this renders the claims unclear to the skilled person (to support a rejection under 35 U.S.C. § 112, second paragraph).

Additionally, Applicants note that the statements made by Examiner Bhatti with respect to this rejection appear to suggest that it would be necessary to identify the displayed peptide that

binds the proteinaceous target for the claims to be acceptable. Applicants respectfully submit that this appears to reflect a misunderstanding of the invention. After all, if the identity of a peptide that binds is already known, why would the skilled person use a method to identify it as binding?

Furthermore, this rejection appears to be contradictory to the rejection of claims 1, 3, and 5-10 over Kruif et al. in view of van Oirschot et al. (WO 91/04986) and/or Geysen (WO 84/03564) as presented on pages 8-10 of the Office Action (a full response to which is discussed further below). The substance of this prior art based rejection appears to be that it would be obvious to practice the claimed invention even without being limited to any particular protein target and with a variety of possible binding peptides from ligands (e.g. antibodies) against the target. If the skilled person would find it obvious to perform a method as alleged in this rejection, how can the claims be simultaneously lacking in enablement or be indefinite to that same skilled person?

Accordingly, Applicants respectfully submit that this rejection may be properly withdrawn because no *prima facie* showing has been made to support either or both rejections as alleged.

Prior art rejections under 35 U.S.C. § 102 and 103(a)

Claims 1, 5-7 and 10 are rejected under 35 U.S.C. § 102(b) as allegedly being clearly anticipated by Ladner et al. (WO 92/15677). Applicants have carefully reviewed the statement of the rejection and respectfully submit that no *prima facie* case of anticipation has been presented.

A review of the reference shows that it is directed to the display of peptides on the surface of a genetic package (see pages 45-70) and use thereof to identify peptides that bind a target of interest (see pages 72-74).

The statements in the rejection assert that page 6, lines 34-35 of Ladner et al. disclose the synthesis of pentapeptides on solid supports. This passage, however, is in a section entitled "Description of the Related Art" and concerns the activities of "Lam et al." There is simply no disclosure of using such immobilized pentapeptides with peptides displayed on the surface of a replicable display package as recited in the claims. This deficiency is a failure to disclose a recited element of the invention as encompassed by claims 1, 5-7 and 10.

MPEP 2131 and the cases cited therein reiterate the well settled standard that anticipation requires that a reference teach every element of a claim. In light of the above identified deficiency in Ladner et al., Applicants respectfully submit that no *prima facie* case of anticipation has been presented and request that this rejection be withdrawn.

Claims 1 and 3 are rejected under 35 U.S.C. § 102(b) as allegedly being clearly anticipated by Mehta et al. (WO 92/08738) or its U.S. equivalent of Ishikawa (USP 5,236,849). Applicants have carefully reviewed the statement of the rejection and respectfully submit that no *prima facie* case of anticipation has been presented.

Applicants again point out that neither reference discloses the use of a display package to display peptides or the contact of such displayed peptides with oligopeptides on a solid phase.

A review of page 17, lines 5-17, as suggested in the rejection shows that Mehta et al. disclosed the use of antibodies in Western blotting of various subfragments of recombinant HCV (hepatitis C virus) proteins. But these proteins were not synthesized on a solid support and the antibodies used in the Western blotting are not peptides displayed on the surface of a replicable display package.

These references thus fail to disclose recited elements of the invention as encompassed by claims 1 and 3. As noted above, no anticipation is possible if a reference does not teach every element of a claim. In light of the above identified deficiencies, Applicants respectfully submit that no *prima facie* case of anticipation has been presented and request that this rejection be withdrawn.

Claims 1 and 3 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Barsomian et al. (WO 95/15982). Applicants have carefully reviewed the statement of the rejection and respectfully submit that no *prima facie* case of obviousness has been presented.

As asserted by the statements in the rejection, Barsomian et al. is alleged to disclose the contacting of displayed peptides with an immobilized target antigen (page 29, lines 30-32). These immobilized antigens are asserted as meeting the claim limitation of "oligopeptides derived from" a proteinaceous target. But as noted previously, the reference differs from the claimed invention at least in that it completely fails to disclose the synthesis of oligopeptides on

a solid phase as required by the claims. The reference only discloses the use of single target antigens without synthesizing them on a solid phase.

The statements include the assertion that one skilled in the art "would be motivated to modify the Barsomian et al. reference because of the motivation to generate a powerful method for rapidly selecting antibodies with the desired specificities and include a further step to synthesize an oligopeptide on a solid phase derived from the target antigen...and further contact the antibodies with the oligopeptide". As such, the asserted motivation appears to be for generating "a powerful method for rapidly selecting antibodies with desired specificities".

But the disclosure on page 29, lines 30-32, already provide such a "powerful method" because the antigen in its entirety, which would include all the epitopes that would be likely to be bound by the displayed antibodies. To alter this by using oligopeptides derived from the antigen would not improve this method because some, if not many or all, of such oligopeptides would **not** have conformations that recognized by the antibodies. Such oligopeptides would be more likely to have only a portion of the epitope recognized by individual antibodies, which would decreased the likelihood that they would be bound by the antibodies. This would result in a less effective, and less "powerful" method to identify antibodies.

Moreover, the reliance of a more "powerful method" appears to be based upon recognition of the power of the instantly claimed invention. This reflects the likelihood that the rejection relies impermissibly on hindsight reconstruction based upon the instant application.

In light of the above, and contrary to the rejection's assertion, the teachings of Barsomian et al. would teach away from the use of oligopeptides derived from a whole antigen because of the loss of epitopes bound by antibodies. Moreover, the asserted motivation appears to rely upon hindsight gained by the availability of the instant disclosure. Applicants therefore respectfully submit that no *prima facie* case of obviousness has been presented and request that this rejection be withdrawn.

Claims 1, 3 and 5-10 are rejected under 35 U.S.C. § 102(b) as allegedly unpatentable over Kruif et al. Applicants have carefully reviewed the statement of the rejection and respectfully submit that no *prima facie* case of obviousness has been presented.

As asserted in the statement of the rejection, Kruif et al. is alleged to disclose the limitations of the claims and as "suggest[ing] the synthesizing of one or more oligopeptide

'derived from a protein target' on a substrate for screening a phage library peptide ligand." Applicants understand this to be recognition that Kruif et al. do not expressly teach the synthesis of an oligopeptide on a solid support (which is supported by the statement on page 9, paragraph 22 of the Office Action). If so, then Kruif et al. cannot have disclosed the contacting of such an immobilized oligopeptide with displayed peptides. As noted above, anticipation requires that a reference teach every element of a claim.

Given the above identifies deficiencies, Kruif et al. cannot anticipate the claimed invention.

Additionally, and in the interest of correcting the record, the statement on page 8, lines 6-8 of the Office Action appears to relate to page 102, column **2**, of Kruif et al., which refers to "solid-phase-bound antigens" **but not** "antigens which are synthesized on solid-phase" as asserted in the Action.

Claims 1, 3 and 5-10 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Kruif et al. in view of van Oirschot et al. (WO 91/04986) and/or Geysen (WO 84/03564). Applicants have carefully reviewed the statement of the rejection and respectfully submit that no *prima facie* case of obviousness has been presented.

As an initial matter, and as noted above, this rejection appears contradictory to the rejections under 35 U.S.C. § 112, first and second paragraphs noted above. How can the claimed invention be obvious to a skilled person at the time of the invention without the benefit of the instant application if it was not enabled for the skilled person at the time of the invention **even with** the instant application? Similarly, how can the claimed invention be unclear to the skilled person if the invention would have been obvious to him/her?

An additional matter should be noted for the record as discussed above with respect to Kruif et al. The statement on page 9, lines 2-4, of the Office Action is identical to the statement on page 8, lines 6-8, of the Action noted above as correctly relating to page 102, column **2**, of Kruif et al. Furthermore, the statement refers to "solid-phase-bound antigens" **but not** "antigens which are synthesized on solid-phase" as asserted in the Action

Turning to the substance of the instant rejection, page 9, paragraph 22, of the Office Action assert that Kruif et al. "fails to specifically disclose, making a plurality of oligopeptide

fragments of a target protein for phage screening." Paragraph 23 then goes on to assert that methods for the production of oligopeptide fragments is known in the art.

Paragraph 24 then asserts that Oirschot et al. teach the use of oligopeptides of a glycoprotein 1 to produce monoclonal antibodies and these oligopeptides are synthesized and arranged on a nitrocellulose strip for binding to a labeled antibody.

Page 10, paragraph 25, then asserts that Geysen teaches a method of detecting subsequences of an antigen that are antigenically active by contacting the subsequences with antibody against the protein.

Paragraph 26 then asserts that it would have been obvious to combine the teachings of Kruif et al. with that of Oirschot et al. or Geysen "and screen the oligopeptides using its corresponding ligand (e.g. antibody) in conventional screening assays in order to determine optimal binding oligopeptide compounds (e.g. epitopes) as suggested in the Kruif reference". Applicants understand this last assertion to include motivation for the combination, which is based on Kruif et al. and the possibility of additional antibody specificities based on using portions of a molecule for selection of antibody fragments.

But Oirschot et al. add nothing to this assertion beyond demonstrating that peptides of a protein can be made and used to produce antibodies which can be verified as binding to the peptides immobilized on a nitrocellulose strip. This just relates to the use of portions of a molecule to make more antibodies.

On the other hand, Geysen is directed to the reverse concept of determining what subsequence of an antigen is "antigenically active" or "the antigenic determinant" (see for example the first paragraph on page 1 of Geysen). The focus is thus to determine what portion of an antigen is recognized by a given antibody as opposed to the use of the portions to generate additional antibodies. With such a focus, there would be no motivation to combine it with the teachings of Kruif et al. because contacting the portions of an antigen with the plurality of antibody fragments of Kruif et al would not help determine what portion of an antigen is responsible for antigenicity. Therefore, the combination would go against the intent of Geysen et al. to find determinants of antigenicity.

Moreover, where is the motivation to use the immobilization approach of Geysen in combination with the teachings of Kruif et al? After all, the generation of additional specificities

that is at the core of Kruif et al. can be done simply by the use of individual portions, for example as taught by Oirschot et al.

Applicants respectfully submit that no motivation has been provided for combining Geysen with the other two references in the instant rejection and that no motivation exists because such a combination would destroy the intent of Geysen. Therefore, the instant rejection appears to be a hindsight reconstruction based upon the instant application. Applicants therefore respectfully submit that no *prima facie* case of obviousness has been presented and request that this rejection be withdrawn.

CONCLUSION

In light of the above amendments and remarks, Applicants believe that the claims are in condition for allowance and urge passage of the application to issue. The Examiner is invited to contact Applicants' agent at the number listed below if it would be helpful in any way to resolve any remaining issues.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 313632000600. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

Dated: 9/4, 2002 By: _____

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